PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PAC/22106 WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB2004/005420	International filing date *(day/month/year)* 23.12.2004	Priority date *(day/month/year)* 24.12.2003
International Patent Classification (IPC) or both national classification and IPC C07C215/54		
Applicant CIPLA LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.10.2005	14.03.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Grammenoudi, S Telephone No. +49 89 2399-8324

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB2004/005420

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-17 as originally filed

Claims, Numbers

1-33 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 31,32

   because:

   ☒ the said international application, or the said claims Nos. 31,32 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13, 15-24, 26-28
	No:	Claims	14,25,29-33
Inventive step (IS)	Yes:	Claims	1-13, 15-24, 26-28
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-30,33
	No:	Claims	31,32

2. Citations and explanations

   see separate sheet

D1= US-A-5 382 600
D2= US-A-5 922 914
D3= US-A-2003/199582
D4= WO-A-03/35599
D7= Journal of Organic Chemistry, vol. 63, no. 22, 1998, pages 8067-8070

SECTION III

Claims 31 and 32 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For the assessment of present claims 31 and 32 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

SECTION V

1. The present application relates to tolterodine, compositions and uses thereof, and processes for preparing the same.

2. Claims for products defined in terms of a process of their manufacture are admissible only if the products as such fulfil the requirements for patentability, i.e. inter alia that they are new and inventive. A product is not rendered novel merely by the fact that it is produced by means of a new process.
(+)-Tolterodine tartrate, its anticholinergic activity and use in the treatment of uri-nary incontinence is known from the art (see D1, Table 1, substance 4a, column 8, lines 4-6, column 29, lines 8-12; D2, Examples 4 and 5; D3, paragraphs 0073 and 0080, Table 1; D4, page 21, line 19 - page 23, line 13, D7, page 8070, right-hand column, lines 26-52).

Accordiggly, the subject-matter of claims 14, 25 and 29-33 (as far as claims 29-33 refer back to claims 14 and 25) are not novel, thereby not meeting the require-ments of Article 33(2) PCT.

3. Document D1 discloses the racemic free base of tolterodine (cf. D1, Table 1, sub-stance 4) without indicating the physical state thereof. However, it is stated in D7 that the free base of (+)-tolterodine is a colorless oil (cf. D7, page 8070, right-hand column, lines 26-40). The crystalline form of tolterodine free base according to present claims 1-3, 13 and 24 is therefore deemed novel in view of the prior art, This also apply to processes for producing this form (claims 4-12 and 15-23). The intermediates of claims 26-28 differ from 3-(2-methoxy-5-methylphenyl)-3-phenyl-propanol which represents the structurally closest compound of the art (cf. D1, Example 3e) by having a benzyl protecting group (intermediate V) or hydrogen (intermediate VI) instead of methyl.
Thus, the subject-matter of claims 1-13, 15-24 and 26-28 fulfil the requirements of Article 33(2) PCT.

4. The problem to be solved by the present application with respect to the cited do-cuments is to provide alternative tolterodine. There is no suggestion in the state of the art that the free base of tolterodine can exist in crystalline form which is ad-vantageous for pharmaceutical use and handling. The subject-matter of claims 1-13, 15-24 involves an inventive step and hence meets the requirements of Arti-cle 33(3) PCT.

5. The intermediates of claims 26-28 are nesessary for carrying out the processes according to present claims 21-23. They satisfy the requirements of Art. 33(3) PCT as well.

6. Although claims 1, 2, 13 and 24 have been drafted as separate independent claims, they relate effectively to the same subject-matter and differ from each other only with regard to the definition of the subject-matter for which protection is sought. As a result, the aforementioned claims lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection. Hence, claims 1, 2, 13 and 24

do not meet the requirements of Article 6 PCT.

7. The chemical name of intermediate 2 on page 12 is obviously erroneous (Art. 6 PCT)

8. (+)-Tolterodine has the R configuration according to the commonly recognised Cahn-Ingold-Prelog system (cf. D2, Examples 4 and 5). Consequently, the desi-gnation used in Examples 3 and 4 of the present invention is incorrect (Art. 6 PCT).

9. The term "about" in connection with ranges (cf. claims 2, 10, 11 and 16, pages 4, 6, 7, 11 and 17) as well as the phrases "and the like" (cf. pages 10 and 11) and "or the like" (cf. pages 9 and 10) render the scope of the application unclear (Art. 6 PCT).

10. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D7 is not mentioned in the description, nor is/are this/these document/s identified therein.